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L2 ANSWER 1 OF 365 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:76313 HCAPLUS
DOCUMENT NUMBER: 142:175353
TITLE: Antigenic epitopes of regulatory protein of virulence factor in *Staphylococcus aureus* and their mimotopes for use as antiinfective agents and vaccines
INVENTOR(S): Shao, Ningsheng; Yang, Guang; Liu, Chuan; Gao, Yaping; Dong, Jie; Ding, Hongmei; Shen, Beifen
PATENT ASSIGNEE(S): Institute of Basic Medical Sciences, Academy of Military Medical Sciences, Peop. Rep. China; Hainan GT-Uniput Pharmaceutical Co. Ltd.
SOURCE: PCT Int. Appl., 16 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005007683	A1	20050127	WO 2003-CN827	20030927
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: CN 2003-150203 A 20030721
AB This invention relates to two antigenic epitopes of regulatory protein TRAP of virulence factor in *Staphylococcus aureus* and their mimotopes. The sequence of the antigenic epitopes are NPTHQLQFSASDT and SYFERYLYPIKE. The mimotope of the antigenic epitopes are XPXHHQHXTGFT or SWFDXXLYPXXX, in which X is any one of 21 kinds of natural L type amino acids D type isomer. The antigenic epitopes and mimotopes can be used as vaccines or medicines to prevent or treat *staphylococcus aureus* infection.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 365 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:14417 HCAPLUS
DOCUMENT NUMBER: 142:112450
TITLE: Peptides antagonistic to anti-angiogenic or .alpha.V integrin antibody for drug screening and treatment of angiogenesis-related disease such as cancer and inflammation
INVENTOR(S): Shealy, David; Wu, Sam; Chen, Yan; Baker, Audrey
PATENT ASSIGNEE(S): Centocor, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000871	A2	20050106	WO 2004-US19898	20040622
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

PRIORITY APPLN. INFO.:

US 2003-480667P P 20030623

AB The invention concerns antagonists of .alpha.V-contg. integrins which have therapeutic activity in oncol. applications and methods for selecting such antagonists using a peptide which competes for alphaV-integrin binding with a known monoclonal antibody having demonstrated anti-tumor activity. The claimed peptide represents a conformational epitope or mimotope present on the ligand to which the therapeutic antibodies selectively bind.

L2 ANSWER 3 OF 365 HCPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2005:108538 HCPLUS

TITLE: A Novel Peptide Isolated from a Phage Display Peptide Library with Trastuzumab Can Mimic Antigen Epitope of HER-2

AUTHOR(S): Jiang, Beihai; Liu, Wenbin; Qu, Hong; Meng, Lin; Song, Shumei; Ouyang, Tao; Shou, Chengchao

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Beijing Institute for Cancer Research and Peking University School of Oncology, Beijing, 100034, Peop. Rep. China

SOURCE: Journal of Biological Chemistry (2005), 280(6), 4656-4662

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Trastuzumab, a humanized antibody to HER-2, has been shown to be effective in the treatment of breast cancer in which HER-2 overexpression and metastasis occurs. In the authors' search for an effective mimic epitope of HER-2 binding with trastuzumab and to develop HER-2 peptide vaccine, the authors screened a phage display 12-mer peptide library with trastuzumab as the target. A mimetic peptide (mimotope) H98 (LLGPYELWELSH) that could specifically recognize trastuzumab was isolated. The DNA encoding peptide H98 was cloned and expressed as the fusion protein GST-H98 in Escherichia coli BL21. The purified GST-H98 could specifically bind to trastuzumab and block the binding of trastuzumab to HER-2 protein. Moreover, H98 could significantly block the function of trastuzumab inhibiting the growth of cancer cells. Mice that were immunized with GST-H98 made specific antibody to H98 as well as to HER-2. In addn., T-cell proliferation occurred in mice immunized with GST-H98. Although no sequence homol. was found between H98 and HER-2, through the use of structure anal. the authors were able to det. that peptide H98 contributed to a conformational epitope of HER-2. Furthermore, the authors detd. that the last two amino acids at the C terminus, and the third together with the fourth amino acid at the N terminus of peptide H98 are crit. to the binding of H98 to trastuzumab. As a result, the authors conclude that peptide H98 has potential for being developed as a HER-2 vaccine for biotherapy of cancer with HER-2 overexpression.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 365 HCPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2005:196173 HCPLUS

TITLE: Using a baculovirus display library to identify MHC class I mimotopes

AUTHOR(S): Wang, Yibing; Rubtsov, Anatolya; Heiser, Ryan; White, Janice; Crawford, Frances; Marrack, Philippa; Kappler, John W.

CORPORATE SOURCE: Howard Hughes Medical Institute, Integrated Department of Immunology, National Jewish Medical and Research Center, Denver, CO, 80206, USA

SOURCE: Proceedings of the National Academy of Sciences of the

PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have developed a baculovirus-based display system for identifying antigen mimotopes for MHC class I-specific T cells. The mouse MHC class I mol., Dd, was displayed on baculovirus-infected insect cells with a library of 9- and 10-mer peptides tethered via a flexible linker to the N terminus of β .2 microglobulin. As a test case, the library was screened by flow cytometry by using a multimeric fluorescent $\alpha\beta$.TCR from a mouse T cell specific for Dd plus an unknown self peptide. A mimotope was identified that, when bound to Dd, stimulated the T cell to secret IL-2. The sequence of the mimotope was used to identify a self peptide present in a mouse protein, Spin. The Spin peptide, when complexed with Dd, also activated the T cell. This technique should be generally useful in identifying and manipulating MHC class I peptide mimotopes and epitopes.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 365 HCPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:204339 HCPLUS
TITLE: Targeting carbohydrate antigens in HIV vaccine development
AUTHOR(S): Pashov, Anastas; Canziani, Gabriela; MacLeod, Stewart; Plaxco, Jason; Monzavi-Karbassi, Behjatolah; Kieber-Emmons, Thomas
CORPORATE SOURCE: Department of Pathology, ACRC 824, UAMS, University of Arkansas for Medical Sciences, 4301 Markham Street, Little Rock, AR, 72205, USA
SOURCE: Vaccine (2005), 23(17-18), 2168-2175
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Peptide mimotopes provide a strategy to augment human immunodeficiency virus 1 (HIV-1) specific carbohydrate reactive immune responses. Their antigenic and immunol. properties will depend on the optimization of motif clustering and multimerization. We observe that structural variants of the same mimetic motif, linear vs. cyclic, can be used to tune the properties of the antibodies elicited. The expansion of the database of mimotope sequence motifs can be increased by analyzing structures that bind to HIV directed monoclonal antibody 2G12 and the lectin Con A (Con A), fostering new mimotope designs. Such anal. indicates that these reagents bind to subsets of mannosyl antigens on the envelope (env) protein.

L2 ANSWER 6 OF 365 HCPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2005:4023 HCPLUS
TITLE: Intranasal immunisation using recombinant Lactobacillus johnsonii as a new strategy to prevent allergic disease
AUTHOR(S): Scheppeler, Lorenz; Vogel, Monique; Marti, Pamela; Mueller, Lorenz; Miescher, Sylvia M.; Stadler, Beda M.
CORPORATE SOURCE: Institute of Immunology, Inselspital, Bern, 3010, Switz.
SOURCE: Vaccine (2005), 23(9), 1126-1134
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have previously demonstrated the induction of a specific anti-IgE response in vivo by parenteral immunization of rhesus monkeys using short IgE mimotopes or an anti-idiotypic antibody mimicking an IgE epitope. Such specific anti-IgE responses may be of clin. benefit for atopic patients. In this study, we examd. the potential for a more convenient therapy via mucosal immunization using live recombinant Lactobacillus johnsonii (Lj) as a vaccine delivery vehicle. Either an anti-idiotypic

scFv or an IgE **mimotope** were expressed on the surface of Lj as fusion proteins using the cell wall anchored proteinase PrtB from *Lactobacillus delbrueckii* subsp. *bulgaricus*. The recombinant Lj were shown to express the heterologous fusion proteins and were specifically recognized by the corresponding anti-human IgE monoclonal antibody. S.c. and intranasal immunization of mice with recombinant Lj, expressing these fusion proteins induced a systemic IgG response against human IgE. Our data suggest that recombinant *Lactobacilli* expressing IgE epitopes may represent a novel means of vaccination to induce a beneficial anti-IgE response.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 365 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2005:8143 HCAPLUS

DOCUMENT NUMBER: 142:216881

TITLE: Vaccination with a Human High Molecular Weight Melanoma-Associated Antigen **Mimotope** Induces a Humoral Response Inhibiting Melanoma Cell Growth In Vitro

AUTHOR(S): Wagner, Stefan; Hafner, Christine; Allwardt, Dorothée; Jasinska, Joanna; Ferrone, Soldano; Zielinski, Christoph C.; Scheiner, Otto; Wiedermann, Ursula; Pehamberger, Hubert; Breiteneder, Heimo

CORPORATE SOURCE: Bio Life Science, Vienna, Austria

SOURCE: Journal of Immunology (2005), 174(2), 976-982

CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Peptide mimics of a conformational epitope that is recognized by a mAb with antitumor activity are promising candidates for formulations of anticancer vaccines. These **mimotope** vaccines are able to induce a polyclonal Ab response focused to the determinant of the mAb. Such attempts at cancer immunotherapy are of special interest for malignant melanoma that is highly resistant to chemotherapy and radiotherapy. In this study, we describe for the first time the design and immunogenicity of a vaccine contg. a **mimotope** of the human high m.w. melanoma-assocd. Ag (HMW-MAA) and the biol. potential of the induced Abs. Mimotopes were selected from a pVIII-9mer phage display peptide library with the anti-HMW-MAA mAb 225.28S. The **mimotope** vaccine was then generated by coupling the most suitable candidate **mimotope** to tetanus toxoid as an immunogenic carrier. Immunization of rabbits with this vaccine induced a specific humoral immune response directed toward the epitope recognized by the mAb 225.28S on the native HMW-MAA. The induced Abs inhibited the in vitro growth of the melanoma cell line 518A2 up to 62%. In addn., the Abs mediated 26% lysis of 518A2 cells in Ab-dependent cellular cytotoxicity. Our results indicate a possible application of this **mimotope** vaccine as a novel immunotherapeutic agent for the treatment of malignant melanoma.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 365 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2005:64552 HCAPLUS

DOCUMENT NUMBER: 142:175310

TITLE: **Mimotope**-hormesis and mortalin/grp75/mthsp70: a new hypothesis on how infectious disease-associated epitope mimicry may explain low cancer burden in developing nations

AUTHOR(S): Deocaris, Custer C.; Taira, Kazunari; Kaul, Sunil C.; Wadhwa, Renu

CORPORATE SOURCE: Cell Proliferation Research Team, Gene Function Research Center, National Institute of Advanced Industrial Science & Technology, Tsukuba Science City, 305-8562, Japan

SOURCE: FEBS Letters (2005), 579(3), 586-590

CODEN: FEBLAL; ISSN: 0014-5793

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal
LANGUAGE: English

AB It is generally obsd. that countries with heavy infectious burden show lower cancer incidence as compared to more affluent nations. With the emerging paradigm on microbial heat shock proteins (hsp70) as mol. link between infections and autoimmune diseases, we posit a new hypothesis, the "**mimotope**-hormesis", on the immunol. impact of infections on regional cancer prevention. According to this, assaults of infection during early adulthood could fortify the immune system to evoke more potent defenses against late-onset diseases, such as cancer, via autoimmunity. Interestingly, both exptl. and clin. data support the beneficial role of autoimmunity in long-term cancer survivors. We illustrate this by a comprehensive *in silico* **mimotope** (epitope mimicry) anal. of human infectious pathogens against mortalins (mthsp70/PB74/GRP75), a type of hsp70 protein involved in control of cell proliferation, immortalization and tumorigenesis.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 365 HCPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2005:25830 HCPLUS
DOCUMENT NUMBER: 142:132619
TITLE: A peptide **mimotope** of type 8 pneumococcal capsular polysaccharide induces a protective immune response in mice
AUTHOR(S): Buchwald, Ulrike K.; Lees, Andrew; Steinitz, Michael; Pirofski, Liise-anne
CORPORATE SOURCE: Department of Medicine, Division of Infectious Diseases, Albert Einstein College of Medicine, Bronx, NY, USA
SOURCE: Infection and Immunity (2005), 73(1), 325-333
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Increasing antibiotic resistance and a rising patient population at risk for infection due to impaired immunity underscore the importance of vaccination against pneumococci. However, available capsular polysaccharide vaccines are often poorly immunogenic in patients at risk for pneumococcal disease. The goal of this study was to explore the potential of peptide mimotopes to function as alternative vaccine antigens to elicit a type-specific antibody response to pneumococci. The authors used a human monoclonal IgA antibody (NAD) to type 8 *Streptococcus pneumoniae* capsular polysaccharide (type 8 PS) to screen a phage display library, and the phage PUB1 displaying the peptide FHLPPYNHNWFAL was selected after three rounds of biopanning. Inhibition studies with phage-displayed peptide or the peptide PUB1 and type 8 PS showed that PUB1 is a mimetic of type 8 PS. PUB1 conjugated to tetanus toxoid (PUB1-TT) induced a type 8 PS-specific antibody response in BALB/c mice, further defining it as a **mimotope** of type 8 PS. The administration of immune sera obtained from PUB1-TT-immunized mice earlier (days 14 and 21) and later (days 87 and 100) after primary and reimmunization resulted in a highly significant prolongation of the survival of naive mice after pneumococcal challenge compared to controls. The survival of PUB1-TT-immunized mice was also prolonged after pneumococcal challenge nearly 4 mo after primary immunization. The efficacy of PUB1-TT-induced immune sera provides proof of principle that a **mimotope**-induced antibody response can protect against pneumococci and suggests that peptide mimotopes selected by type-specific human antibodies could hold promise as immunogens for pneumococci.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 365 HCPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 2004:1063879 HCPLUS
DOCUMENT NUMBER: 142:132596
TITLE: Isolation and structural analysis of peptide mimotopes for the disialoganglioside GD2, a neuroblastoma tumor antigen

AUTHOR(S):

Foerster-Waldl, Elisabeth; Riemer, Angelika B.; Dehof, Anna Katharina; Neumann, Dirk; Braemswig, Kira; Boltz-Nitulescu, George; Pehamberger, Hubert; Zielinski, Christoph C.; Scheiner, Otto; Pollak, Arnold; Lode, Holger; Jensen-Jarolim, Erika

CORPORATE SOURCE:

Department of Pediatrics and Juvenile Medicine, Medical University of Vienna, Austria

SOURCE:

Molecular Immunology (2005), 42(3), 319-325
CODEN: MOIMD5; ISSN: 0161-5890

PUBLISHER:

Elsevier B.V.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The disialoganglioside GalAcbeta1-4(NeuAcalpha2-8NeuAcalpha2-3)Galbeta1-4Glcbeta1-1Cer (GD2) is expressed on various tumors, including neuroblastoma, and was defined as a relevant tumor antigen. The monoclonal anti-GD2 antibody 14.18 is widely used for diagnostic purposes in neuroblastoma, and in its mouse/human chimeric form (ch14.18) now enters passive immunotherapy regimens in phase II clin. trials. This study aimed to generate structural mimics of the 14.18 epitope of GD2. Therefore, we used the ch14.18 antibody for selecting immunoreactive GD2 peptide mimotopes from a decamer phage display library. In all, 13 GD2 peptide mimics could be detd. by biopanning and their specificity was demonstrated by exclusive recognition by the ch14.18 antibody. Furthermore, their nature of being GD2 mimics and their degree of mimicry was confirmed by competition with the natural antigen. When performing a comparative visualization of the GD2 epitope and selected mimotopes using a three-dimensional computer modeling system (BALLView), we demonstrated fitting of the GD2 mol. and the mimotopes in the antigen-binding pouch of a GD2 specific antibody. Moreover, the computer modeling argued for optimal affinity of the GD2 mimotopes. We thus provide evidence that the generation of GD2 peptide mimotopes is successful when using the neuroblastoma antibody ch14.18 for selection, and that this approach might offer a tool to develop a vaccination strategy against this malignant pediatric tumor.

REFERENCE COUNT:

25

THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s mimotope and mimetope

L3 0 MIMOTOPE AND MIMETOPE

=> s mimetope

L4 18 MIMETOPE

=> dup rem 14

PROCESSING COMPLETED FOR L4

L5 15 DUP REM L4 (3 DUPLICATES REMOVED)

=> d 15 1-5 ibib ab

L5 ANSWER 1 OF 15 HCPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2005:166672 HCPLUS

DOCUMENT NUMBER: 142:238612

TITLE: Receptor editing in peripheral B cell tolerance

AUTHOR(S): Rice, Jeffrey S.; Newman, Jeffrey; Wang, Chuansheng; Michael, Daniel J.; Diamond, Betty

CORPORATE SOURCE: Departments of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2005), 102(5), 1608-1613

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Receptor editing or secondary Ig gene rearrangement occurs in immature, autoreactive B cells to maintain self-tolerance. Here the authors show that nonspontaneously autoimmune mice immunized with a peptide mimotope of DNA develop peptide- and DNA-reactive antibodies.

Antigen-specific B cells display a follicular B cell phenotype. As these

cells move into the memory compartment, many express RAG protein and acquire expression of both .kappa. and .lambda. light chains. Thus, this study provides evidence for receptor editing occurring in a mature, antigen-activated B cell population. Because the receptor editing obsd. here occurred in an autoreactive response to antigen, it may function to maintain peripheral tolerance.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:606350 HCAPLUS

DOCUMENT NUMBER: 141:150981

TITLE: Methods for preventing and treating Alzheimer's disease (AD) using N-terminal A.beta.42 peptide vaccines

INVENTOR(S): Mattner, Frank

PATENT ASSIGNEE(S): Austria

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004062556	A2	20040729	WO 2004-EP162	20040113
WO 2004062556	A3	20040916		
WO 2004062556	C1	20041021		
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ				
PRIORITY APPLN. INFO.:			AT 2003-36	A 20030114
			AT 2003-1464	A 20030917

OTHER SOURCE(S): MARPAT 141:150981

AB The invention relates to the use of a compd. comprising the following amino acid sequence X1X2X3X4X5X6, wherein X1 is an amino acid, except of C, X2 is an amino acid, except of C, X3 is an amino acid, except of C, X4 is an amino acid, except of C, X5 is an amino acid, except of C, X6 is an amino acid, except of C, and wherein X1X2X3X4X5X6 is not DAEFRH, said compd. having a binding capacity to an antibody being specific for the natural N-terminal A.beta.42 sequence DAEFRH, and 5-mers thereof having a binding capacity to said antibody being specific for the natural N-terminal A.beta.42 sequence DAEFRH, for the prepn. of a vaccine for Alzheimer's disease. Mimotopes of DAEFRH were identified by screening 6-mer peptide libraries for binding to an antibody to DAEFRH.

L5 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2003:306488 HCAPLUS

DOCUMENT NUMBER: 138:400244

TITLE: The Naive B Cell Repertoire Predisposes to Antigen-Induced Systemic Lupus Erythematosus

AUTHOR(S): Wang, Chuansheng; Khalil, Magi; Ravetch, Jeffrey; Diamond, Betty

CORPORATE SOURCE: Department Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA

SOURCE: Journal of Immunology (2003), 170(9), 4826-4832

CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB It is clear that the development of an autoimmune disease usually depends on both a genetic predisposition and an environmental trigger. In this study, we demonstrate that BALB/c mice develop a lupus-like serol. following immunization with a peptide **mimotope** of DNA, while

DBA/2 mice do not. We further demonstrate that the crit. difference resides within the B cell compartment and that the naive B cell repertoire of DBA/2 mice has fewer B cells specific for the DNA **mimotope**. Differences in the strength of B cell receptor signaling exist between these two strains and may be responsible for the difference in disease susceptibility. BALB/c mice possess more autoreactive cells in the native repertoire; they display a weaker response to Ag and exhibit less Ag-induced apoptosis of B cells. DBA/2 mice, in contrast, display a stronger B cell receptor signal and more stringent central tolerance. This correlates with resistance to lupus induction. Thus, the degree to which autoreactive B cells have been eliminated from the naive B cell repertoire is genetically regulated and may det. whether a nonspontaneously autoimmune host will develop autoimmunity following exposure to Ag.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 15 HCPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2003:566860 HCPLUS

DOCUMENT NUMBER: 139:148059

TITLE: Using peptide mimotopes to elucidate anti-polysaccharide and anti-nucleic acid humoral responses

AUTHOR(S): Caton, M.; Diamond, B.

CORPORATE SOURCE: Dept. of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA

SOURCE: Cellular and Molecular Biology (Paris, France, Print) (2003), 49(2), 255-262

CODEN: CMOBEF; ISSN: 0145-5680

PUBLISHER: CMB Association

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Humoral responses against polysaccharide or nucleic acid antigens are often difficult to characterize and to induce. For example, the eliciting antigen for the development of anti-double-stranded(ds)DNA antibodies is unclear. DsDNA is a poor immunogen, yet antibodies to it bear the hallmark of a T cell dependent response. The microbial origin of polysaccharide antigens is, in general, readily known, but these antigens often do not elicit B cell memory responses, which are crucial for vaccine development. This review focuses on the use of peptide mimotopes to better understand humoral responses against non-protein antigens. First, the authors describe a **mimotope** for dsDNA that was derived by probing a peptide phage library with an anti-dsDNA antibody. The authors discuss the usefulness of this **mimotope** in a search for candidate protein antigens and for examg. the phenotype of antigen-specific B cells. Next, the authors discuss two mimotopes for phosphorylcholine (PC), a component of *S. pneumoniae* C polysaccharide. One was derived through mapping an anti-idiotype epitope and the other by probing a phage-display peptide library with an anti-PC antibody. Both of these peptide mimotopes for PC provide useful information regarding the requirements of a protective antibody response against pneumococcal infection, and define a crit. role for adjuvant and carrier as well as **mimotope**.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 15 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:711602 SCISEARCH

THE GENUINE ARTICLE: 712KG

TITLE: Differential effects of interleukin-4 in peptide induced autoimmunity

AUTHOR: Deocharan B; Marambio P; Edelman M; Putterman C (Reprint)

CORPORATE SOURCE: Albert Einstein Coll Med, Div Rheumatol, Dept Med, Ullamnn 1223, 1300 Morris Pk Ave, Bronx, NY 10461 USA (Reprint); Albert Einstein Coll Med, Div Rheumatol, Dept Med, Bronx, NY 10461 USA; Winthrop Univ Hosp, Dept Pathol, Mineola, NY 11501 USA; Albert Einstein Coll Med, Dept Microbiol & Immunol, Bronx, NY 10461 USA

COUNTRY OF AUTHOR: USA
SOURCE: CLINICAL IMMUNOLOGY, (AUG 2003) Vol. 108, No. 2, pp. 80-88

Publisher: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST,
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ISSN: 1521-6616.

DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 36

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB BALB/c mice immunized with multimeric DWEYSVWLSN develop IgG1 anti-DNA antibodies and glomerular immunoglobulin deposits, leading us to investigate the role of IL-4 in this model of antigen induced lupus. Splenocytes from DWEYSVWLSN immunized mice secreted IL-4 but not gamma-interferon. Following peptide immunization, IgG1 anti-peptide and anti-DNA antibodies were significantly higher in IL-4 wild type mice, while IgM and IgG3 anti-DNA levels were significantly higher in IL-4 knockout mice. Titers of IgG anti-laminin and anti-histone, but not anti-Sm/RNP and anti-cardiolipin antibodies, were significantly higher in the IL-4 wild type group. Glomerular immunoglobulin deposition was substantially decreased in IL-4 knockout mice. We conclude that while IL-4 does not materially affect the generation of some autoantibody responses associated with peptide induced autoimmunity, IL-4 deficiency inhibits kidney immunoglobulin deposition. The effect of IL-4 on humoral autoimmunity in lupus is complex, and is dependent on genetic background, the antigenic trigger and stage of disease. (C) 2003 Elsevier Science (USA). All rights reserved.

=> s mimotope and definition
L6 14 MIMOTOPE AND DEFINITION

=> dup rem 16
PROCESSING COMPLETED FOR L6
L7 8 DUP REM L6 (6 DUPLICATES REMOVED)

=> d 17 1-8 ibib ab

L7 ANSWER 1 OF 8 HCPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:107702 HCPLUS
DOCUMENT NUMBER: 140:337437
TITLE: Allergen mimotopes
AUTHOR(S): Riemer, Angelika; Scheiner, Otto; Jensen-Jarolim, Erika
CORPORATE SOURCE: General Hospital Vienna, Institute of Pathophysiology, University of Vienna, Vienna, 1090, Austria
SOURCE: Methods (San Diego, CA, United States) (2004), 32(3), 321-327
CODEN: MTHDE9; ISSN: 1046-2023
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The causative treatment of type I allergies is a long pursued goal in immunol. To design safe and efficient vaccine preps., the interaction of the allergen and the symptom-inducing IgE antibodies still needs to be better understood. In this article, the authors describe the use of the phage display technique in allergy. It yields epitope mimics, so-called mimotopes, which can be employed for both, investigation of allergen-IgE interactions and definition of safe novel vaccines.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:531686 SCISEARCH
THE GENUINE ARTICLE: 691KG
TITLE: Strategies in cancer vaccines development
AUTHOR: Cunتو-Amesty G; Monzavi-Karbassi B; Luo P; Jousheghany F; Kieber-Emmons T (Reprint)

CORPORATE SOURCE: Univ Arkansas Med Sci, Dept Pathol, Ctr Canc Res, 4301 W Markham St, Slot 824, Little Rock, AR 72205 USA (Reprint); Univ Arkansas Med Sci, Dept Pathol, Ctr Canc Res, Little Rock, AR 72205 USA; Univ Penn, Dept Pathol, Philadelphia, PA 19104 USA

COUNTRY OF AUTHOR: USA
SOURCE: INTERNATIONAL JOURNAL FOR PARASITOLOGY, (MAY 2003) Vol. 33, No. 5-6, pp. 597-613.

Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
ISSN: 0020-7519.

DOCUMENT TYPE: General Review; Journal

LANGUAGE: English

REFERENCE COUNT: 164

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The recent **definition** of tumour-specific immunity in cancer patients and the identification of tumour-associated antigens have generated renewed enthusiasm for the application of immune-based therapies for the treatment of malignancies. Recent developments in cancer vaccines have also been based on an improved understanding of the cellular interactions required to induce a specific anti-tumour immune response. Consequently, a number of cancer vaccines have entered clinical trials. Targeting broad-spectrum tumour-associated antigens has emerged as a strategy to lower the risk of tumour escape due to the loss of specific nominal antigen. Amongst the most challenging of tumour-associated antigens to which to target in active specific immunotherapy applications are carbohydrate antigens. As carbohydrates are intrinsically T-cell-independent antigens, more novel approaches are perhaps needed to drive specific-T-cell-dependent immune responses to carbohydrate antigens. In this context peptide mimetics of core structures of tumour-associated carbohydrate antigens might be developed to augment immune responses to these broad-spectrum antigens. (C) 2003 Australian Society for Parasitology Inc. Published by Elsevier Science Ltd. All rights reserved.

L7 ANSWER 3 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:602755 SCISEARCH

THE GENUINE ARTICLE: 221JF

TITLE: Towards the pathogenesis of autoimmune liver disease

AUTHOR: Mackay I R (Reprint); Davies J M; Rowley M J

CORPORATE SOURCE: MONASH UNIV, DEPT BIOCHEM & MOL BIOL, WELLINGTON RD, CLAYTON, VIC 3168, AUSTRALIA (Reprint)

COUNTRY OF AUTHOR: AUSTRALIA

SOURCE: JOURNAL OF AUTOIMMUNITY, (AUG 1999) Vol. 13, No. 1, pp. 163-169.

Publisher: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON NW1 7DX, ENGLAND.

ISSN: 0896-8411.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 22

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB There have been recent improvements in the clinical understanding and **definition** of the major types of autoimmune liver disease. However, still lacking is knowledge of their prevalence and pathogenesis. Three areas of study are in progress in our laboratory. First, in type 1 autoimmune hepatitis, the search continues to identify a liver/disease-specific autoantigenic reactant. Using hepatocyte membrane preparations, immunoblotting has underlined the problem of distinguishing, among multiple reactants, those that may be causally rather than consequentially related to hepatocellular damage. Second, in primary biliary cirrhosis (PBC), the need for population screening to ascertain prevalence and detect preclinical cases can be met by a rapid automated procedure for detection, by specific enzyme inhibition in microtitre wells, of antibody (anti-M2) to the pyruvate dehydrogenase complex E2 subunit (PDC-E2). Third, the structure of the conformational epitope within the inner lipoyl domain of PDC-E2 is being investigated by screening random phage-displayed peptide libraries using PBC sera. This

has yielded phage clones in which the sequence of the peptide insert portrays the structure of this epitope, as judged by clustering of PBC-derived sequences to particular branches of a guide-tree that shows relatedness of peptides, and by reactivity of selected phage clones with anti-PDC-E2. Thus phage display identifies a peptide '**mimotope**' of the antibody epitope in the inner lipoyl domain of PDC-E2. (C) 1999 Academic Press.

L7 ANSWER 4 OF 8 HCPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 1997:730007 HCPLUS

DOCUMENT NUMBER: 128:33477

TITLE: **Definition of the primary structure of hepatitis B virus (HBV) pre-S hepatocyte binding domain using random peptide libraries**

AUTHOR(S): D'Mello, Felicity; Partidos, Charalambos D.; Steward, Michael W.; Howard, Colin R.

CORPORATE SOURCE: Department of Pathology and Infectious Diseases, Royal Veterinary College, London, NW1 0TU, UK

SOURCE: Virology (1997), 237(2), 319-326

CODEN: VIRLAX; ISSN: 0042-6822

PUBLISHER: Academic

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The pre-S-specific monoclonal antibody MA 18/7 has been shown to inhibit the binding of HBV to HepG2 cells and liver membranes. This antibody can thus be used to identify the crit. residues of the pre-S region involved in the hepatocyte-binding domain. Using overlapping 7-mer peptides representing the pre-S region of HBV, the epitope recognized by MA 18/7 was shown to contain sequences from both the pre-S1 and pre-S2 regions, thus indicating that the hepatocyte-binding domain is conformationally dependent. To further characterize the primary structure of the hepatocyte-binding domain on the pre-S protein, a phage-displayed 15-mer peptide library and a 8-mer solid phase peptide library were used to analyze the fine specificity of the monoclonal antibody MA 18/7. Several mimotopes were identified with the phage-displayed peptide library, the majority of which possess a central motif with at least 3 identical residues present within the native pre-S1 sequence. No significant consensus sequences were found when these mimotopes were compared to the pre-S2 sequence. Mimotopes identified using the solid-phase peptide library also contained a similar motif. All phage mimotopes and a single **mimotope** from the solid-phase peptide library competed with recombinant HBsAg particles contg. the pre-S1 region for binding to MA 18/7. Mouse antisera raised against 4 mimotopes from the phage display library reacted with HBsAg particles contg. pre-S sequences. The data show that the structure of the pre-S mol. around the conserved DPAF motif in the pre-S region may have a functional role in binding HBV to cellular receptors, and that the central motif identified in mimotopes of this region may offer a novel strategy target for the improvement of existing hepatitis B vaccines which, at present, are mostly devoid of pre-S specificities.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 8 HCPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 1995:959111 HCPLUS

DOCUMENT NUMBER: 124:6900

TITLE: **Mapping the Ig superantigen-binding site of HIV-1 gp120**

AUTHOR(S): Goodlick, Lee; Zevit, Noam; Neshat, Mehran S.; Braun, Jonathan

CORPORATE SOURCE: Dep. Pathol., Univ. California, Los Angeles, CA, 90095, USA

SOURCE: Journal of Immunology (1995), 155(11), 5151-9

CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The envelope glycoprotein, gp120, of HIV-1 has recently been identified as a member of the new family of Ig superantigens (Ig-SAg). This

classification is based on the selective binding of gp120 to an unusually high proportion of endogenous, nonimmune Ig, and the selective activation of nonimmune B cells by gp120 in vitro. Many, if not all of the nonimmune Ig that bind to gp120 are members of the VH3 Ig gene family. The aim of this study was to det. the epitope on gp120 that was responsible for its Ig-SAg binding activity. To do this, we utilized a panel of 30 peptides derived from gp160 in a competition-binding assay. For five Ig's that were tested, as well as for polyclonal serum IgM, two overlapping peptides (each 20 amino acids in length) were identified that were potent inhibitors of gp120 binding. Similarly, the 10 amino acid overlap region of these two peptides had inhibitory activity. Thus, this decamer sequence represented the optimal Ig-SAg epitope or mimotope. The amino acid residue at position 1 of the decamer, and to a lesser extent at position 10, was crit. for peptide binding. In addn. to this decamer peptide, other peptides that shared modest sequence homol. were also selectively inhibitory for specific Ig samples. These findings provide the first **definition** of an Ig-SAg ligand at the peptide level and will facilitate further structural and biol. characterization of this new class of pathogenic Ags.

L7 ANSWER 6 OF 8 HCPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 1996:89130 HCPLUS
DOCUMENT NUMBER: 124:172858
TITLE: Synthetic peptide **mimotope** of the CAMPATH-1
(CD52) antigen, a small glucosylphosphatidylinositol-
anchored glycoprotein
AUTHOR(S): Hale, Geoffrey
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, CB2 1QP, UK
SOURCE: Immunotechnology (1995), 1(3,4), 175-87
CODEN: IOTEER; ISSN: 1380-2933
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB CAMPATH-1 (CD52) antibodies are among the most powerful and specific lympholytic agents in humans and have numerous potential applications for human therapy. The CD52 antigen is a GPI-anchored glycoprotein with an exceptionally short peptide sequence of only 12 amino acids and a single, complex, N-linked oligosaccharide. Antibodies bind to the deglycosylated antigen and to a proteolytic fragment, but not to the synthetic peptide alone. Objectives were to characterize the antigenic epitope more precisely and to construct a synthetic analog. Such an analog would be useful for assay and purifn. of the therapeutic CAMPATH-1 antibodies as well as for studies of the antibody-antigen binding site. Collections of synthetic peptides based on the natural sequence were screened with a panel of CD52 antibodies. A synthetic peptide composed of the natural C-terminal amino acids plus two addnl. residues was found to mimic the antigen with sufficient affinity to be useful for a variety of assays and for construction of an affinity matrix for antibody purifn. Systematic mutation of this peptide enabled the **definition** of the crit. residues for antibody binding, which will be of great help in building a model of the antibody-antigen interaction. Peptide mimotopes synthesis using a natural sequence as a starting point, rather than a completely random library, may be useful in many other similar circumstances.

L7 ANSWER 7 OF 8 HCPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 1995:998760 HCPLUS
DOCUMENT NUMBER: 124:84195
TITLE: Selection of peptide ligands for the antimucin core antibody C595 using phage display technology:
definition of candidate epitopes for a cancer vaccine
AUTHOR(S): Laing, P; Tighe, P; Kwiatkowski, E; Milligan, J;
Price, M; Sewell, H
CORPORATE SOURCE: University Hospital, Queens Medical Centre,
Nottingham, NG7 2UH, UK
SOURCE: Clinical Molecular Pathology (1995), 48(3), M136-M141
CODEN: CMPAFI; ISSN: 1355-2910
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors tried to further define the specificity of the antimucin core antibody C595 by fitting it with a family of hexapeptide ligands by immunoselection of filamentous bacteriophage from a gene III display library of approx. 6.4.times.10⁷ random hexapeptides. Three rounds of immunoselection were used to enrich for C595 binding phage. DNA sequencing revealed the hexapeptides expressed. Bacteriophage and corresponding synthetic hexapeptides were used in ELISA assay to det. binding affinities. Twenty nine clones from this selected population were analyzed. Seven contained the natural epitope RPAP, encoded by two different DNA sequences; 17/29 contained the motif RLPP. In all, 28/29 clones contained the motif RXXP and one clone (RVRPAP) contained the motif RXXP in two peptidic registers; 24/28 clones (6/8 DNA sequences) contained a hydrophobic residue (V or I) at position 1 relative to the RXXP motif. In addn. the proximity of RXXP to glycine (position 5) suggests that this contributes in the natural epitope to antibody/antigen binding, which was not detected by chem. synthetic methods. One clone, KSKAGV, bears no obvious relation to the natural epitope and therefore qualifies as a weakly binding mimotope. This approach has rapidly defined the specificity of this antibody in unprecedented detail, and provides a more comprehensive mol. basis for exploring the immune recognition of the MUC1 mucin by the C595 antibody. Importantly, the novel but related epitopes seen provide peptide specificities and a strategy which may prove useful in generating cancer vaccine candidates.

L7 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 1995:540268 HCAPLUS

DOCUMENT NUMBER: 123:141292

TITLE: Characterization of epitopes on human p53 using phage-displayed peptide libraries: insights into antibody-peptide interactions

AUTHOR(S): Stephen, Charles W.; Helminen, Paivi; Lane, David P.

CORPORATE SOURCE: CRC Cell Transformation Research Group, Univ. of Dundee, DD1 4HN, UK

SOURCE: Journal of Molecular Biology (1995), 248(1), 58-78
CODEN: JMOBAK; ISSN: 0022-2836

PUBLISHER: Academic

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors previously described the use of a phage-displayed library of random hexapeptides to define and localize the epitope on the human tumor suppressor protein p53 recognized by the monoclonal antibody PAb240. Here the authors have extended these results to a further eight anti-p53 monoclonal antibodies and to two further libraries, which display 12-mer and 20-mer peptides, resp. First, the authors showed that selection of PAb240 binding clones from the 12-mer and 20-mer libraries gives essentially identical results to those obtained by screening the 6-mer library. Second, the authors used the 6-mer and 12-mer libraries to define the detailed specificity profiles of six antibodies (DO-1, DO-2, DO-7, Bp53-11, Bp53-12 and Bp53-19), which recognize the same short, highly immunogenic N-terminal segment of p53. Finally, the authors employed all three libraries to reveal the distinct mechanisms by which PAb421 and PAb122, two monoclonal antibodies that allosterically activate sequence-specific DNA binding by p53, react specifically with the same pos.-charged C-terminal segment. In each case the epitope locations inferred from the selected sequences were confirmed by probing an array of overlapping synthetic peptides representing the primary sequence of p53. The results emphasize the consequences for epitope mapping of screening random, as opposed to antigen-derived, peptide libraries, specifically (1) that comparison of selected sequences reveals the contribution of individual residues to binding energy and specificity; (2) that heteroclitic reactions can lead to **definition** of a consensus that is related to but distinct from the immunizing epitope and (3) that isolation of non-immunogen-homologous "mimotope" sequence reveals discrete, alternative ligand structures. The results with PAb421 and PAb122 provide examples where, while selection from the 12-mer and 20-mer libraries leads to isolation of immunogen-homologous sequences, selection from the 6-mer library results in the isolation either of no binding clones (PAb122) or solely of "mimotope" sequences with

no discernible homol. to the original antigen (PAb421). In addn. the results with PAb421 reveal that linear epitopes can be longer than previously thought and can be formally discontinuous, consisting of independent contact motifs, which show promiscuous relative positioning.

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=> s mimotope is defined
L8          0 MIMOTOPE IS DEFINED

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L9          0 MIMETOPE IS DEFINED

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L10         0 MIMETOPE DEFINITION

=> s mimetope and definition
L11         0 MIMETOPE AND DEFINITION
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FILE 'HCAPLUS, SCISEARCH' ENTERED AT 15:17:47 ON 29 MAR 2005

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L1      508 S MIMOTOPE
L2      365 DUP REM L1 (143 DUPLICATES REMOVED)
L3      0 S MIMOTOPE AND MIMETOPE
L4      18 S MIMETOPE
L5      15 DUP REM L4 (3 DUPLICATES REMOVED)
L6      14 S MIMOTOPE AND DEFINITION
L7      8 DUP REM L6 (6 DUPLICATES REMOVED)
L8      0 S MIMOTOPE IS DEFINED
L9      0 S MIMETOPE IS DEFINED
L10     0 S MIMETOPE DEFINITION
L11     0 S MIMETOPE AND DEFINITION
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L12     18 MIMETOPE
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